

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

WITTE, WELLER & PARTNER
Attn. Otten, Hajo
Postfach 105462
D-70047 Stuttgart
GERMANY

WITTE, WELLER & PARTNER
Patentanwälte

24. März 2003

Frist: 20.04.03

notiert: SW

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

20/03/2003

Applicant's or agent's file reference

3605P118WO HO/gf

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/EP 02/03730

International filing date
(day/month/year)

04/04/2002

Applicant

NMI NATURWISSENSCHAFTLICHES UND...

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bruno Danti

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 3605P118W0 H0/gf	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 02/ 03730	International filing date (day/month/year) 04/04/2002	(Earliest) Priority Date (day/month/year) 10/04/2001
Applicant NMI NATURWISSENSCHAFTTLICHES UND...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/03730

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/53 G01N33/543

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, MEDLINE, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ✓	WO 00 63701 A (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 26 October 2000 (2000-10-26) abstract page 2, line 29 -page 4, line 21 page 14, line 6 -page 15, line 12 example 1	1-18
X ✓	WO 00 39587 A (ILLUMINA, INC.) 6 July 2000 (2000-07-06) claims 1-19 abstract	11-14
Y	page 41, line 11-23; examples 1-4	1-10, 15-18

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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

7 March 2003

Date of mailing of the international search report

20/03/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Thumb, W

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/03730

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
✓ X ✓	WO 00 11214 A (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 2 March 2000 (2000-03-02) page 3, line 11-24 page 11, line 1-31	11-14
Y	page 27, line 13 -page 28, line 25	1-10, 15-18
✓ X ✓	WO 99 35293 A (LYNX THERAPEUTICS, INC.) 15 July 1999 (1999-07-15) page 27, line 20 -page 32, line 29 examples 1-4	11-14
Y		1-10, 15-18
✓ X ✓	MENDOZA L G ET AL: "HIGH-THROUGHPUT MICROARRAY-BASED ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA)" BIOTECHNIQUES, EATON PUBLISHING, NATICK, US, vol. 27, no. 4, October 1999 (1999-10), pages 778,780,782-786,788, XP000992893 ISSN: 0736-6205 the whole document	11-14
A		1-10, 15-18
✓ X ✓	WO 97 42507 A (ISIS INNOVATION LIMITED) 13 November 1997 (1997-11-13) the whole document	11-14
A		1-10, 15-18
✓ A ✓	US 3 555 143 A (PHARMACIA AB) 12 January 1971 (1971-01-12) the whole document	1-18
✓ A ✓	WO 96 19732 A (MICROGENICS CORPORATION) 27 June 1996 (1996-06-27) the whole document	1-18

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11-14

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to polypeptide and nucleic acid capture reagents.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/03730

B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 11-14
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/03730

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0063701	A	26-10-2000	EP 1169649 A2 JP 2002542487 T WO 0063701 A2	09-01-2002 10-12-2002 26-10-2000
WO 0039587	A	06-07-2000	US 6429027 B1 AU 2391600 A EP 1141712 A1 JP 2002533727 T WO 0039587 A1 US 2002187515 A1	06-08-2002 31-07-2000 10-10-2001 08-10-2002 06-07-2000 12-12-2002
WO 0011214	A	02-03-2000	US 6291190 B1 AU 5394699 A EP 1108060 A1 WO 0011214 A1 US 2002176873 A1	18-09-2001 14-03-2000 20-06-2001 02-03-2000 28-11-2002
WO 9935293	A	15-07-1999	US 6265163 B1 AU 754929 B2 AU 2113999 A CA 2317695 A1 EP 1054999 A2 HU 0100242 A2 JP 2002500050 T NO 20003531 A PL 342114 A1 WO 9935293 A2 US 6511802 B1	24-07-2001 28-11-2002 26-07-1999 15-07-1999 29-11-2000 28-06-2001 08-01-2002 05-09-2000 21-05-2001 15-07-1999 28-01-2003
WO 9742507	A	13-11-1997	WO 9742507 A1	13-11-1997
US 3555143	A	12-01-1971	SE 343949 B AT 283590 B BE 699352 A CH 484426 A CS 159223 B2 DE 1598945 A1 DK 123795 B ES 341257 A1 FI 48508 B FR 1527279 A GB 1192784 A NL 6707479 A , B NO 126594 B US RE29474 E	20-03-1972 10-08-1970 01-12-1967 15-01-1970 27-12-1974 01-04-1971 31-07-1972 01-10-1968 01-07-1974 31-05-1968 20-05-1970 04-12-1967 26-02-1973 15-11-1977
WO 9619732	A	27-06-1996	AU 2949795 A EP 0745222 A1 JP 2935578 B2 JP 9508707 T WO 9619732 A1 US 5919642 A	10-07-1996 04-12-1996 16-08-1999 02-09-1997 27-06-1996 06-07-1999

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

Otten, Hajo
WITTE, WELLER & PARTNER
Postfach 105462
D-70047 Stuttgart
ALLEMAGNE

WITTE, WELLER & PARTNER

Patentanwälte

27. Aug. 2003

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Frist:

notiert:

Date of mailing
(day/month/year)

26.08.2003

Applicant's or agent's file reference
3605P118WO HQ/sw

IMPORTANT NOTIFICATION

International application No.
PCT/EP02/03730

International filing date (day/month/year)
04.04.2002

Priority date (day/month/year)
10.04.2001

Applicant
NMI NATURWISSENSCHAFTLICHES UND MEDIZIN-...et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Brandt, M

Tel. +49 89 2399-2926



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3605P118WO HO/sw	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP02/03730	International filing date (<i>day/month/year</i>) 04.04.2002	Priority date (<i>day/month/year</i>) 10.04.2001
International Patent Classification (IPC) or both national classification and IPC G01N33/48		
Applicant NMI NATURWISSENSCHAFTLICHES UND MEDIZIN-...et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18.10.2002	Date of completion of this report 26.08.2003
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized Officer Thumb, W Telephone No. +49 89 2399-7350



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP02/03730**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-13 as originally filed

Claims, Numbers

1-11 received on 02.08.2003 with letter of 30.07.2003

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP02/03730**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-11
	No: Claims	
Inventive step (IS)	Yes: Claims	1-11
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Claims 1-11, filed with the letter dated 30.7.2003, do not appear to introduce subject-matter which extends beyond the content of the application as originally filed and therefore comply with the provisions of Article 34(2)(b) PCT.
2. Claim 1 meets the requirements of Articles 33(2) and (3) PCT.
Document D1 (WO-A-00/63701) discloses microarrays of polypeptides on a solid support (page 2, line 29 - page 4, line 21). The microarrays of D1 can be used for large scale binding assays in numerous diagnostic and screening applications. Samples may comprise a wide variety of biological fluids. In order to detect bound ligands, a labelled sample may be mixed with a differentially labelled sample in a competition assay. Ratio measurement of signals from different labels is referred to. For many diagnostic and investigative purposes it is useful to measure the levels of ligands, e.g. protein ligands, in blood or serum (page 14, line 6 - page 16, line 31). In an example, differential labelling of protein mixtures with the fluorescent dyes Cy3 and Cy5, followed by binding of a mixture of the two protein pools to a capture reagent array (antibodies) is shown. Quantification of the proteins based on the results obtained from competitive binding reactions is shown (Example 1, page 17, line 25 et seq.; see in particular Results section, page 20 et seq.).
The subject-matter of claim 1 differs from the teaching of D1 in that after the competitive reaction of an analyte with its analogue and detection of the amount of bound competitor/analogue the total amount of bound molecules (analyte and analogue) is determined using a further detection reagent.
Two color detection of analytes bound to capture molecules after a competitive reaction is well known in the art (see for example D2: WO-A-00/39587, page 41, paragraph 3; D3: WO-A-00/11214, page 28).
However, the state of the art does not contain any indication that would prompt the skilled person to perform a sandwich-type detection of the total amount of bound analyte and competitor using a further binding detection reagent following competitive binding to capture reagents.
Claim 1 and dependent claims 2-6 therefore meet the requirements of Articles 33(2) and (3) PCT.
3. Claim 7 refers to a kit comprising capture molecules, competitor/analogue

molecules, **and** detection reagents for analyte and for competitor/analogue molecules.

Following the argumentation put forward under item 2., it would not be obvious for the skilled person to combine reagents for a competitive **and** a sandwich detection assay in one kit.

Claim 7 and dependent claims 8-10 therefore also meet the requirements of Articles 33(2) and (3) PCT.

4. Claims 10 and 11 refer to the use of arrays of beads having attached thereto capture molecules in a method according to any of claims 1-6 and thus also meet the requirements of Articles 33(2) and (3) PCT.

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Claims

1. A method for determining the concentration/amount of analyte molecules in a sample, comprising the steps of:
 - a) adding to the sample a known concentration/amount of competitor/analogue molecules of the analyte, said competitor/analogue molecules being distinct from said analyte molecules,
 - b) reacting/contacting the sample of step a) with capture molecules for the analyte and competitor/analogue molecules,
 - c) determining the amount of competitor/analogue molecules bound to the capture molecules using a detection reagent, preferably a labeled or (enzyme) conjugated ligand, or labeled competitor/analogue molecules, and determining the total amount of analyte and competitor/analogue molecules bound to the capture molecules using a detection reagent, preferably a labeled or (enzyme) conjugated ligand, and calculating therefrom a measure for the ratio R of analyte and competitor/analogue molecules that are bound to the capture molecules,

- d) determining the concentration/amount of the analyte molecules from the ratio R of step c) and the known concentration/amount of competitor/analogue molecules in the sample of step a).
2. The method of claim 1, wherein in step c) the amount of competitor/analogue molecules bound to the capture molecules is determined distinct but parallel to the determination of the total amount of competitor/analogue and analyte molecules bound to the capture molecules.
3. The method of claim 1 or 2, wherein in step b) analyte and competitor/analogue molecules not reacted with/bound to the capture molecules are removed, preferably by washing steps.
4. The method of any of claims 1 - 3, wherein the method is performed on an array of immobilised capture molecules.
5. The method of any of claims 1 - 3, wherein the method is performed in a suspension of beads having attached thereto capture molecules.
6. The method of any of claims 1 - 5, wherein the competitor/analogue molecules are labeled with a fluorescent dye.
7. Kit for performing the method of any of claims 1 - 6, comprising capture molecules, competitor/analogue molecules, and detection reagents for analyte and for competitor/analogue molecules.

8. The kit of claim 7, wherein the capture molecules are arranged in an array, preferably a microarray.
9. The kit of claim 7 or 8, wherein the capture molecules are attached to beads.
10. Use of a suspension/virtual array of beads having attached thereto capture molecules for determining the concentration/amount of at least one species of analyte molecules, in a method as in any of claims 1 - 6.
11. Use according to claim 10, wherein said beads have attached thereto different species of capture molecules for determining different species of analyte molecules.